FDA Approves Lilly's EBGLYSS™ (lebrikizumab-lbkz) for Adults and Children 12 Years and Older with Moderate-to-Severe Atopic Dermatitis

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EBGLYSS provides a new first-line biologic treatment for moderate-to-severe atopic dermatitis that is not well controlled with topicals

Patients treated with EBGLYSS experienced significant skin clearance as early as four weeks and meaningful itch relief as early as two weeks

EBGLYSS delivers long-lasting efficacy for patients through one year of treatment with a monthly maintenance dose

INDIANAPOLIS, Sept. 13, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today the U.S. Food and Drug Administration (FDA) approved EBGLYSS™ (lebrikizumab-lbkz), a targeted IL-13 inhibitor, for the treatment of adults and children 12 years of age and older who weigh at least 88 pounds (40 kg) with moderate-to-severe atopic dermatitis (eczema) that is not well controlled despite treatment with topical prescription therapies.[1] Eczema inflammation under the skin can lead to symptoms seen and felt on the outside. EBGLYSS works by targeting eczema inflammation throughout the body that can lead to dry, itchy and irritated skin.

EBGLYSS 250 mg/2 mL injection can be used with or without topical corticosteroids and is dosed as a single monthly maintenance injection following the initial phase of treatment. The recommended initial starting dose of EBGLYSS is 500 mg (two 250 mg injections) at Week 0 and Week 2, followed by 250 mg every two weeks until Week 16 or later when adequate clinical response is achieved; after this, maintenance dosing is a single monthly injection (250 mg every four weeks).[1] View the EBGLYSS patient photos here.

"Patients still struggle to control their moderate-to-severe atopic dermatitis with currently available therapies. Many experience poor long-term disease control, and severe itch can significantly impact their daily lives," said Jonathan Silverberg, M.D., Ph.D., M.P.H., professor of dermatology at George Washington University School of Medicine and Health Sciences in Washington, DC, and first author of the *New England Journal of Medicine* manuscript summarizing EBGLYSS clinical trials.[2] "Today's FDA approval of EBGLYSS is a big win for patients, as we now have a new first-line biologic treatment option for moderate-to-severe disease when topical prescriptions aren't enough."

The approval was based on results from the ADvocate 1, ADvocate 2, and ADhere studies, which included over 1,000 adults and children (aged 12 and older) with moderate-to-severe eczema who were unable to control their symptoms with topical prescription medicines. The primary endpoint for these studies was evaluated at 16 weeks and measured clear or almost clear skin (IGA 0,1).[1]

In an average of two studies (ADvocate 1 and 2), 38 percent of people who took EBGLYSS achieved clear or almost-clear skin at 16 weeks (versus 12 percent with placebo) and 10 percent saw these results as early as four weeks.[1,3] Of the people who experienced clear or almost-clear skin at Week 16, 77 percent maintained those results at one year with once-monthly dosing. Forty-eight percent of responders who were switched from EBGLYSS to placebo at Week 16 maintained these results at one year.[4]

Similarly, in both studies, many people experienced itch relief with EBGLYSS. On average, 43 percent of people who took EBGLYSS felt itch relief at 16 weeks (compared to 12 percent who took placebo) and five percent felt relief as early as two weeks.[1,5] Of the people who felt itch relief at Week 16, 85 percent still felt that relief at one year of treatment with monthly maintenance dosing. Sixty-six percent of responders who were switched from EBGLYSS to placebo at Week 16 maintained these results at one year.[4]

"Eczema can affect people of all skin tones, ethnicities, genders and ages. Nearly 16.5 million adults in the U.S. have eczema, with 6.6 million experiencing moderate-to-severe symptoms like itchiness, dry and scaly skin, discoloration and rashes, which can lead to more scratching that may cause skin to crack and bleed,"[6] said Kristin Belleson, President and CEO of the National Eczema Association. "The approval of EBGLYSS provides hope and promise for the eczema community and those still seeking lasting relief from disruptive symptoms."

The most common side effects of EBGLYSS include eye and eyelid inflammation, such as redness, swelling and itching; injection site reactions and shingles (herpes zoster). EBGLYSS cannot be used in people allergic to lebrikizumab-lbkz or to any of the ingredients in EBGLYSS. The maintenance period was generally consistent with the 16-week safety profile throughout multiple studies. **See the Safety Summary below and full Prescribing Information**.[1]

"People living with eczema have symptoms that can appear at the most inopportune times, creating unpredictability and impacting their everyday lives," said Daniel Skovronsky, M.D., Ph.D., chief scientific officer and president of Lilly Research Laboratories, and president, Lilly Immunology. "Today's approval allows people the opportunity to reimagine life with eczema as EBGLYSS offers a targeted approach to reduce a main cause of eczema inflammation. EBGLYSS provides long-lasting symptom relief with a convenient once-monthly maintenance dose."

EBGLYSS will be available in the United States in the coming weeks. Lilly is committed to setting new expectations for patients living with eczema and is working with insurers, health systems and providers to enable patient access to EBGLYSS. Through Lilly Support Services™ for EBGLYSS™, Lilly will offer a patient support program including co-pay assistance for eligible, commercially insured patients.

EBGLYSS was approved for use by the European Commission in 2023, as well as in Japan in January 2024 with additional markets expected later this year.

Lilly has exclusive rights for development and commercialization of EBGLYSS in the U.S. and the rest of the world outside Europe. Lilly's partner Almirall S.A. has licensed the rights to develop and commercialize EBGLYSS for the treatment of dermatology indications, including eczema,

in Europe.

View the EBGLYSS brand logo and product photos here and here.

About ADvocate 1 and ADvocate 2
ADvocate 1 and ADvocate 2 are 52-week randomized, double-blind, placebo-controlled, parallel-group, global, Phase 3 studies designed to evaluate EBGLYSS as monotherapy in adults and children (aged 12 to less than 18 years of age and weighing at least 40 kg) with moderate-to-severe eczema.

During the 16-week treatment induction period, patients received EBGLYSS 500-mg initially and at two weeks, followed by EBGLYSS 250-mg or placebo every two weeks. In the maintenance period, patients with moderate-to-severe eczema who achieved a clinical response after 16 weeks of EBGLYSS treatment were re-randomized to receive EBGLYSS every two weeks or four weeks or placebo for an additional 36 weeks. Patients who required rescue treatment during the induction period or who did not meet protocol-defined response criteria at 16 weeks received open-label EBGLYSS every two weeks for an additional 36 weeks.

The primary endpoint was measured by an Investigator Global Assessment (IGA) score of clear (0) or almost clear (1) skin with a reduction of at least two points from baseline at 16 weeks. Key secondary endpoints were measured by Eczema Area and Severity Index (EASI) and the Pruritus Numeric Rating Scale. EASI measures extent and severity of the disease.

About ADhere
ADhere is a 16-week randomized, double-blind, placebo-controlled, parallel-group, global, Phase 3 study to evaluate the efficacy and safety of EBGLYSS in combination with topical corticosteroids (TCS) initiated in 211 adults and children (aged 12 to less than 18 years of age and weighing at least 40 kg) with moderate-to-severe eczema. In the study, patients' baseline eczema symptoms were inadequately controlled by topical medications.

INDICATION AND SAFETY SUMMARY
EBGLYSS™ (EHB-glihs) is an injectable medicine used to treat adults and children 12 years of age and older who weigh at least 88 pounds (40 kg) with moderate-to-severe eczema (atopic dermatitis) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies. EBGLYSS can be used with or without topical corticosteroids.

It is not known if EBGLYSS is safe and effective in children less than 12 years of age or in children 12 years to less than 18 years of age who weigh less than 88 pounds (40 kg).

Warnings - Do not use EBGLYSS if you are allergic to lebrikizumab-lbkz or to any of the ingredients in EBGLYSS. See the Patient Information leaflet that comes with EBGLYSS for a complete list of ingredients.

Before using
Before using EBGLYSS, tell your healthcare provider about all your medical conditions, including if you:

- Have a parasitic (helminth) infection.
- Are scheduled to receive any vaccinations. You should not receive a "live vaccine" if you are treated with EBGLYSS.
- Are pregnant or plan to become pregnant. It is not known if EBGLYSS will harm your unborn baby. If you become pregnant during treatment with EBGLYSS, you or your healthcare provider can call Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979) to report the pregnancy.
- Are breastfeeding or plan to breastfeed. It is not known if EBGLYSS passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Possible side effects
EBGLYSS can cause serious side effects, including:

- **Allergic reactions. EBGLYSS can cause allergic reactions that may sometimes be severe.** Stop using EBGLYSS and tell your healthcare provider or get emergency help right away if you get any of the following signs or symptoms:
  - breathing problems or wheezing
  - itching
  - swelling of the face, lips, mouth, tongue or throat
  - fainting, dizziness, feeling lightheaded
  - skin rash
  - hives
  - cramps in your stomach area (abdomen)
- **Eye problems.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision, such as blurred vision.

The most common side effects of EBGLYSS include:

- eye and eyelid inflammation, including redness, swelling, and itching
- injection site reactions
- shingles (herpes zoster)

These are not all of the possible side effects of EBGLYSS. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

How to take

- **See the detailed "Instructions for Use" that comes with EBGLYSS for information about how to prepare and inject EBGLYSS and how to properly store and throw away (dispose of) used EBGLYSS prefilled pens and prefilled syringes.**
- Use EBGLYSS exactly as prescribed by your healthcare provider.
- EBGLYSS is given as an injection under the skin (subcutaneous injection).
- If your healthcare provider decides that you or a caregiver can give the injections of EBGLYSS, you or a caregiver should receive training on the right way to prepare and inject EBGLYSS. Do not try to inject EBGLYSS until you have been shown the right way by your healthcare provider. In children 12 years of age and older, EBGLYSS should be given by a caregiver.
- If you miss a dose of EBGLYSS, inject the missed dose as soon as possible, then inject your next dose at your regular scheduled time.

Learn more
EBGLYSS is a prescription medicine available as a 250 mg/2 mL injection prefilled pen or prefilled syringe. For more information, call **1-800-545-5979** or go to **ebglyss.lilly.com**

This summary provides basic information about EBGLYSS but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking to your doctor. Be sure to talk to your doctor or other healthcare provider about EBGLYSS and how to take it. Your doctor is the best person to help you decide if EBGLYSS is right for you.

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About EBGLYSS
EBGLYSS is a monoclonal antibody that selectively targets and neutralizes IL-13 with high binding affinity and a slow dissociation rate.[1,7,8] EBGLYSS binds to the IL-13 cytokine at an area that overlaps with the binding site of the IL-4Rα subunit of the IL-13Rα1/IL-4Rα heterodimer, preventing formation of this receptor complex and inhibiting IL-13 signaling.[9] IL-13 is implicated as a primary cytokine tied to the pathophysiology of eczema, driving the type-2 inflammatory loop in the skin, and EBGLYSS selectively targets IL-13.[1]

The EBGLYSS Phase 3 program consists of five key global studies evaluating over 1,300 patients, including two monotherapy studies (ADvocate 1 and 2), a combination study with topical corticosteroids (ADhere), as well as long-term extension (ADjoin) and adolescent open label (ADore) studies. Further data results from ADmirable and ADapt are expected to be shared in 2024 and early 2025.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about EBGLYSS (lebrikizumab-lbkz) as a treatment for people with moderate-to severe atopic dermatitis and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, or that EBGLYSS will receive additional regulatory approvals, or be commercially successful. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

[1] EBGLYSS. Prescribing Information. Lilly USA, LLC.

[2] Silverberg J, et al. Two Phase 3 Trials of Lebrikizumab for Moderate-to-Severe Atopic Dermatitis. *N Engl J Med.* 2023 Mar 23;388(12):1080-1091. doi: 10.1056/NEJMoa2206714. Epub 2023 Mar 15. PMID: 36920778.

[3] Data on File. Lilly USA, LLC. DOF-LK-US-0031.

[4] Blauvelt A, et al. Efficacy and safety of lebrikizumab in moderate-to-severe atopic dermatitis: 52-week results of two randomized double-blinded placebo-controlled phase III trials. *B Journal Dermatol.* 2023;188(6):740-748. doi:10.1093/bjd/ljad022

[5] Data on File. Lilly USA, LLC. DOF-LK-US-0033.

[6] Chiesa Fuxench ZC, et al. Atopic Dermatitis in America Study: A Cross-Sectional Study Examining the Prevalence and Disease Burden of Atopic Dermatitis in the US Adult Population. *Journal of Investigative Dermatology.* 2019;139, 583e590; doi:10.1016/j.jid.2018.08.028

[7] Ultsch M, et al. Structural basis of signaling blockade by anti-IL-13 antibody lebrikizumab. *J Mol Biol*. 2013;425(8):1330-1339. doi:10.1016/j.jmb.2013.01.024

[8] Okragly A, et al. Binding, neutralization and internalization of the interleukin-13 antibody, lebrikizumab. *Dermatol Ther (Heidelb).* Published online June 13, 2023. doi:10.1007/s13555-023-00947-7

[9] Bieber T. Interleukin-13: targeting an underestimated cytokine in atopic dermatitis. *Allergy*. 2020;75(1):54-62. doi:10.1111/all.13954

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